UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
CHEMICAL SAFETY
AND POLLUTION
PREVENTION

April 15, 2014

MEMORANDUM

SUBJECT: Efficacy Review for NP 4.5 (D&F) Detergent/Disinfectant;
EPA Reg. No. 1839-95;
DP Barcode: D417488

FROM: Marcus Rindal, Microbiologist
Product Science Branch
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4.15.14

THRU: Mark Perry, Team Leader
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MP

TO: Velma Noble, PM 31/Drusilla Copeland
Regulatory Management Branch I
Antimicrobials Division (7510P)

APPLICANT: Stepan Company
22 West Frontage Road
Northfield, IL 60093

FORMULATION FROM LABEL:

Active Ingredient(s)	% by wt.
Alkyl (60% C_{14}, 30% C_{16}, 5% C_{12}, 5% C_{18}) dimethyl benzyl ammonium chlorides	2.25%
Alkyl (68% C_{12}, 32% C_{14}) dimethyl ethylbenzyl ammonium chlorides	2.25%
Inert Ingredients	95.50%
Total	100.00%

I BACKGROUND

The product, NP 4.5 (D&F) Detergent/Disinfectant (EPA Reg. No. 1839-95), is an EPA-approved disinfectant (bactericide, fungicide, virucide), mildewstat, and deodorizer for use on hard, non-porous surfaces in household, commercial, institutional, industrial, food processing, farm, animal care, and hospital or medical environments. The applicant requested to amend the registration of this product to add new claims for effectiveness as a disinfectant against the public health organisms: *Acinetobacter baumannii* (ATCC 19606), *Enterobacter aerogenes* (ATCC 13048), *Enterococcus faecium* (ATCC 19434), Vancomycin Resistant *Enterococcus faecalis* (ATCC 51299), submission of a new study to support *Enterobacter aerogenes* (ATCC 13048) currently approved for this registration, and addition of the qualified marketing claim: "Kills ESKAPE pathogen group." Studies were conducted at MICROBIOTEST, located at 105 Carpenter Drive in Sterling, VA 20164.

This data package contained a letter from the applicant to EPA (dated December 13, 2013), EPA Form 8570-35 (Data Matrix), three studies (MRID 492760-01, -02, -03), Statements of No Data Confidentiality Claims for all studies, and the proposed label.

II USE DIRECTIONS

The concentrated liquid product is a one-step disinfectant detergent formulated specifically for use in hospitals, nursing homes, schools, food processing plants, food service establishments, transportation terminals, automotive garages, office buildings, manufacturing facilities, lodging establishments, retail businesses, athletic/recreational facilities, sports stadiums, amphitheaters, convention centers, and households. Hard non-porous surfaces to be treated include: appliance exteriors, barber/salon instruments/tools, bathroom fixtures, bathtubs, bed frames, cabinets, cages, carts, chairs, coolers, counter tops, desks, door knobs, exercise equipment, exercise mats, floors, flower buckets, garbage cans and garbage pails, hospital beds, hospital equipment, inflatable plastic structures, kennels, mirrors, outdoor furniture, personal protective safety equipment, picnic tables, racks, shelves, shower curtains, shower stalls, sinks, tables, telephones, toilets, urinals, vanity tops, walls, whirlpools, and windows. The proposed label also indicated that the product may be used on hard, non-porous surfaces, including: glass, glazed ceramic, glazed porcelain, glazed tile, metal (e.g., chrome, stainless steel), plastic, sealed granite, sealed marble, and vinyl. General application methods specify using a mop and bucket, hand pump trigger sprayer, low pressure coarse sprayer, or sponge.

Directions for Disinfectant Activity, Fungicidal Activity, and limited Virucidal Activity: on the proposed label provided the following information regarding preparation and use of the product: Add 2 ounces of the product per gallon of water or 8 ounces of the product per gallon of water to inactivate Canine parvovirus. Apply the use solution with a mop, cloth, sponge, hand pump trigger sprayer or low pressure coarse sprayer. Wet all surfaces thoroughly. Allow surfaces to remain wet for 10 minutes. Remove excess liquid. For heavily soiled areas, a pre-cleaning step is required. For food processing premises, all surfaces in the area must be thoroughly rinsed with potable water. Directions for extended Virucidal Activity is achieved at 8 ounces per gallon or equivalent dilution rate (2812 ppm active quat) on hard non-porous environmental surfaces with a 10 minute contact time.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Disinfectants for Use on Hard Surfaces in Hospital or Medical Environments (Additional Bacteria): Effectiveness of disinfectants against specific bacteria other than those named in the AOAC Use-Dilution Method, AOAC Germicidal Spray Products as Disinfectants Method, AOAC Fungicidal Test, and AOAC Tuberculocidal Activity Method, must be determined by either the AOAC Use-Dilution Method or the AOAC Germicidal Spray Products as Disinfectants Method. Ten carriers must be tested against each specific microorganism with each of 2 product samples, representing 2 different product lots. To support products labeled as "disinfectants" for specific bacteria (other than those bacteria named in the above test methods), killing of the specific microorganism on all carriers is required.

NOTE: Testing at the Nominal Concentration for active(s) is acceptable with the exception of Carbapenem Resistant *Enterobacteriaceae* (CRE)*
**Klebsiella pneumonia* New Dehli Metallo-Beta Lactamase (NDM-1) Carbapenem Resistant.

Supplemental Claims: An antimicrobial agent identified as a "one-step" disinfectant or as effective in the presence of organic soil must be tested for efficacy with an appropriate organic soil load, such as 5 percent serum.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 492760-01 "AOAC Use Dilution Test Supplemental," against *Acinetobacter baumannii* (ATCC 19606) and *Enterobacter aerogenes* (ATCC 13048) for NP 4.5 (D&F) Detergent/Disinfectant, by M. Hamid Bashir. Study conducted at MICROBIOTEST. Study completion date – August 2, 2013. Laboratory Project Identification Number 123-422.

This study was conducted against *Acinetobacter baumannii* (ATCC 19606) and *Enterobacter aerogenes* (ATCC 13048). Two lots (Lot Nos. 4077-003 and 4077-004) of the product, NP 4.5 (D&F) Detergent/Disinfectant, were tested using the AOAC Use-Dilution Method (AOAC Official Methods of Analysis, 18th Edition, 2006) as described in Protocol 123.2.07.07.13. Use solutions were prepared by adding 1 part of the product and 63 parts of sterile deionized water (1:64 dilution). A culture of each challenge microorganism was prepared. Horse serum was added to the culture to achieve a 5% organic soil load. Ten (10) stainless steel penicylinder carriers per product lot were immersed for 15 minutes in a 48-54 hour old suspension of test organism, at a ratio of 20 carriers per tube of 20 mL broth. The carriers were dried for 40 minutes at 36°C. Each carrier was placed in 10 mL of the use solution for 10 minutes at 21°C. The tubes containing the use solution were swirled after addition of the carriers. Following exposure, individual carriers were transferred to Letheen Broth to neutralize. The tubes containing neutralizer were swirled gently for 2-3 rotations avoiding intense swirling or agitation after addition of the carriers. All subcultures were incubated for 48±2 hours at 36±1°C. Following incubation, the subcultures were examined for the presence or absence of visible growth. Controls included those for carrier counts, sterility, viability, neutralizer effectiveness, confirmation of the challenge microorganism, and antibiotic resistance.

2. MRID 492760-02 "AOAC Use Dilution Test Supplemental," against *Enterococcus faecium* (ATCC 19434) for NP 4.5 (D&F) Detergent/Disinfectant, by M. Hamid Bashir.

Study conducted at MICROBIOTEST. Study completion date – September 10, 2013. Laboratory Project Identification Number 123-432.

This study was conducted against *Enterococcus faecium* (ATCC 19434). Two lots (Lot Nos. 4077-003 and 4077-004) of the product, NP 4.5 (D&F) Detergent/Disinfectant, were tested using the AOAC Use-Dilution Method (AOAC Official Methods of Analysis, 18th Edition, 2006) as described in Protocol 123.1.08.28.13. Use solutions were prepared by adding 1 part of the product and 63 parts of sterile deionized water (1:64 dilution). A culture of each challenge microorganism was prepared. Horse serum was added to the culture to achieve a 5% organic soil load. Ten (10) stainless steel penicylinder carriers per product lot were immersed for 15 minutes in a 48-54 hour old suspension of test organism, at a ratio of 20 carriers per tube of 20 mL broth. The carriers were dried for 40 minutes at 36°C. Each carrier was placed in 10 mL of the use solution for 10 minutes at 21°C. The tubes containing the use solution were swirled after addition of the carriers. Following exposure, individual carriers were transferred to Letheen Broth to neutralize. The tubes containing neutralizer were swirled gently for 2-3 rotations avoiding intense swirling or agitation after addition of the carriers. All subcultures were incubated for 48±2 hours at 36±1°C. Following incubation, the subcultures were examined for the presence or absence of visible growth. Controls included those for carrier counts, sterility, viability, neutralizer effectiveness, confirmation of the challenge microorganism, and antibiotic resistance.

3. MRID 492760-03 "AOAC Use Dilution Test Supplemental," against Vancomycin Resistant *Enterococcus faecalis* (ATCC 51299) for NP 4.5 (D&F) Detergent/Disinfectant, by Sean Michael Stuekerjuergen. Study conducted at MICROBIOTEST. Study completion date – November 26, 2013. Laboratory Project Identification Number 123-435.

This study was conducted against Vancomycin Resistant *Enterococcus faecalis* (ATCC 51299). Two lots (Lot Nos. 4077-003 and 4077-004) of the product, NP 4.5 (D&F) Detergent/Disinfectant, were tested using the AOAC Use-Dilution Method (AOAC Official Methods of Analysis, 18th Edition, 2006) as described in Protocol 123.1.11.14.13. Use solutions were prepared by adding 1 part of the product and 63 parts of sterile deionized water (1:64 dilution). A culture of the challenge microorganism was prepared. Non-Heat Inactivated Horse serum was added to the culture to achieve a 5% organic soil load. Ten (10) stainless steel penicylinder carriers per product lot were immersed for 15 minutes in the 48-54 hour old suspension of test organism, at a ratio of 20 carriers per tube of 20 mL broth. The carriers were dried for 40 minutes at 36°C. Each carrier was placed in 10 mL of the use solution for 10 minutes at 20°C. The tubes containing the use solution were swirled after addition of the carriers. Following exposure, individual carriers were transferred to Letheen Broth to neutralize. The tubes containing neutralizer were swirled gently for 2-3 rotations avoiding intense swirling or agitation after addition of the carriers. All subcultures were incubated for 48±2 hours at 36±1°C. Following incubation, the subcultures were examined for the presence or absence of visible growth. Controls included those for carrier counts, sterility, viability, neutralizer effectiveness, confirmation of the challenge microorganism, and antibiotic resistance.

V RESULTS

MRID Number	Organism	No. Exhibiting Growth/ Total No. Tested		Carrier Counts (CFU/ carrier)
		Lot # 4077-003	Lot # 4077-004	
492760-01	*Acinetobacter baumannii*	0/10	0/10	7.7×10^5
	Enterobacter aerogenes	0/10	0/10	8.4×10^4
492760-02	*Enterococcus faecium*	0/10	0/10	1.1×10^6
492760-03	Vancomycin Resistant *Enterococcus faecalis*	0/10	0/10	7.2×10^5

VI CONCLUSIONS

1. The submitted efficacy data (MRID 492760-01) support the use of a 2 oz. per gallon of water dilution of the product, NP 4.5 (D&F) Detergent/Disinfectant, as a disinfectant with bactericidal activity against *Acinetobacter baumannii* and *Enterobacter aerogenes* on hard, non-porous surfaces in the presence of a 5% organic soil load for a 10-minute contact time. Complete killing was observed in the subcultures of the required number of carriers tested against the required number of product lots. Neutralizer effectiveness testing showed positive growth of the microorganism. Viability controls were positive for growth. Sterility controls did not show growth.

2. The submitted efficacy data (MRID 492760-02) support the use of a 2 oz. per gallon of water dilution of the product, NP 4.5 (D&F) Detergent/Disinfectant, as a disinfectant with bactericidal activity against *Enterococcus faecium* on hard, non-porous surfaces in the presence of a 5% organic soil load for a 10-minute contact time. Complete killing was observed in the subcultures of the required number of carriers tested against the required number of product lots. Neutralizer effectiveness testing showed positive growth of the microorganism. Viability controls were positive for growth. Sterility controls did not show growth.

3. The submitted efficacy data (MRID 492760-03) support the use of a 2 oz. per gallon of water dilution of the product, NP 4.5 (D&F) Detergent/Disinfectant, as a disinfectant with bactericidal activity against Vancomycin Resistant *Enterococcus faecalis* on hard, non-porous surfaces in the presence of a 5% organic soil load for a 10-minute contact time. Complete killing was observed in the subcultures of the required number of carriers tested against the required number of product lots. Neutralizer effectiveness testing showed positive growth of the microorganism. Viability controls were positive for growth. Sterility controls did not show growth.

VII RECOMMENDATIONS

1. The proposed label claims that a 1:64 dilution of the product, NP 4.5 (D&F) Detergent/Disinfectant, is an effective disinfectant against *Acinetobacter baumannii, Enterobacter aerogenes, Enterococcus faecium,* and Vancomycin Resistant *Enterococcus faecalis* on hard, non-porous surfaces in the presence of 5%

serum contamination for a 10-minute contact time. These claims are acceptable as they are supported by the submitted data.